

POLYGLYCEROLS AND POLYGLYCEROL ESTERS IN NUTRITION, HEALTH AND DISEASE

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Polyglycerols and polyglycerol esters, as a broad class of compounds, have been used for a number of years as useful and desirable adjuncts in nutrition, health, and in the treatment of certain diseases. The use of these compounds has been limited by their lack of quality and reproducibility in food and medical products that would be submitted for approval to the Food & Drug Administration (FDA). With the process developed by Babayan and issued as U.S. Patent No. 3,637,774, this limitation was overcome. In recent years we have noted the availability of such products and the approval by the FDA and the Codex Alimentarius for the use of polyglycerol esters of fatty acids in foods.

The edible and industrial application of the various polyglycerol esters are appearing in the literature, as well as products which list polyglycerol esters as one of the components in the formulation of the product. It is not surprising that a broad range class of compounds having multi-functionality and flexibility is being considered over an equally broad range of hydrophilic-lipophilic emulsion requirements. A study of their physical and chemical composition and properties is indicative of their unique and useful functionality and applications.

Although in previous presentations and publications¹⁻¹² we have covered the salient characteristics of the polyglycerol esters, it may be useful to briefly summarize the data for the completeness of this presentation.

When glycerine is subjected to heat, in the presence of a catalyst, polymerization takes place. Usually the condensation takes place at temperatures above 20°C with the elimination of water and the formation of an ether linkage between two glycerine molecules. Fig. 1 illustrates this reaction. The condensation reaction involves the α -hydroxyl groups of the glycerine molecule. Subsequent polymerization proceeds with the remaining α -hydroxyl groups and another glycerine molecule to form higher polymers. The reaction under these conditions appears to be linear and a range of polymers can be formed. The reaction can be followed by the amount of water that is formed from the polymerization as well as the changes in refractive index, viscosity figures and birefringency values of the product. Some typical specific gravity and viscosity figures for a range of the polyglycerols is given in Table 1. The polyglycerols of the various polymer ranges are viscous fluids which are water soluble.

The polyglycerols may be converted into polyglycerol esters by direct esterification with a fatty acid or by intermolecular rearrangement with a triglyceride. The polyglycerol formed by the heat polymerization can now be reacted with fatty acids of varying chain length and unsaturation. Fatty acids

TABLE 1. Typical Viscosities and Specific Gravities of Commercially Prepared Polyglycerols

	Polyglycerol	Specific Gravity	65.6° Viscosity, cs.	99°C
Triglycerol	1.379	440	70	
Heptaglycerol	1.383	1300	110	
Decaglycerol	1.390	3200	260	

from acetic to tetracosenoic in the saturated series and/or mono, di and polyunsaturated fatty acids may be used in the direct esterification. The other alternative is to conduct molecular rearrangement with a triglyceride of known composition and structure to a new polyglycerol ester at random distribution. Fig. 2 illustrates the two reactions that may be used in the preparation of the polyglycerol esters. Depending upon the monoglycerols used in the reaction and the condition employed, one is able to prepare partial or neutral esters of a polyglycerol of a given molecular weight and fatty acids and/or triglycerides of known composition. The polyglycerol esters prepared by these approaches constitute the basis for the diversified products that are available for edible, medical and industrial uses. R.T. McNamee summarizes the reactions and their product characteristics recently in an update on the polyglycerol esters.¹³ The effect of the fatty acid chain length and degree of esterification on the hydrophilic-lipophilic balance (HLB) values of the polyglycerol esters is illustrated in Figs. 3, 4 & 5. The range of their specific gravities is given in Fig. 7.

Their hydrophilic-lipophilic ranges is illustrated in Table 2. The wide range of the polyglycerol esters is clearly indicated in these figures and tables and once again re-emphasizes the flexibility and utility of the class as a whole.

Concurrently with the edible and industrial applications and uses of the polyglycerol esters, several pharmaceutical, medical, nutritional and cosmetic groups have been exploring the unique characteristics of the polyglycerol esters.

Since the polyglycerols are water soluble compounds and their viscosity increases with the increase in molecular weight, they become useful components in viscosity control, gravity control and humectants able to carry water and yet maintain the desired consistency of the food or medical formulation.

TABLE 2. HLB Values Calculated from the Theoretical Compositions of Products Formed by Reaction of Stearic Acid with Polyglycerols.

	HLB	Molar Ratio of Stearic Acid : Polyg.
Polyglycerol	1.1	
Triglycerol	6.7 (6.8)	4.9 (5.3)
Heptaglycerol	10.1 (12.2)	8.1 (8.8)
Decaglycerol	12.5 (14.5)	10.6 (11.2)

The partial esters of polyglycerols can be emulsifiers, clouding agents, weighting agents and solvents for a variety of food products. They tend to be multi-functional and do the work of several other additives.

The U.S. Patent No. 4,035,750¹, demonstrates the suitability of such polyglycerol esters in the preparation of beverages. The multi-functional polyglycerol esters not only behave as solvents and carriers for flavoring agents, but also as emulsifiers and clouding agents in such beverage preparations. Depending on the type of beverage desired, one can select the particular polyglycerol ester to bring out the desired characteristics.

The neutral esters of polyglycerols can be, lubricants, crystallization inhibitors, gross additives, and moisture barrier agents, as well as solvents and carriers for oil soluble vitamins, colors and steroids. The ability of polyglycerols and polyglycerol esters to replace fat in foods and yet maintain the satiety and feeling of eating rich fatty foods has been utilized in special dietary products, where more than 50% of the calories have been eliminated without sacrificing the consistency, appearance, and taste of the food. For example, the Weight Watchers imitation ice cream and dietetic dessert contains no fat, but uses the polyglycerol esters to give satiety and to reduce the caloric content of the food.

Above from the unique characteristic of being able to replace or eliminate fat from a formula, the polyglycerol esters also tend to reduce the actual caloric metabolic yield of a food. If we assume that the entire molecule of the polyglycerol mono-ester of a fatty acid is completely metabolized, a decaglyceryl mono-ester for example, would contribute 56.5 kcal/c in contrast to the 9.2 kcal/c for fats. If, however, the polyglycerol backbone is not completely metabolized and only the fatty acid moiety is utilized, then the same compound would have less than 2 kcal/c. Illustrating the two cleavage points which are in question in the metabolic fate of the polyglycerols and polyglycerol esters. Our data has indicated that the polyglycerols and polyglycerol esters are quantitatively metabolized and utilized in both animal and human studies². Several other investigators, primarily Michaels and Coons³, have argued that the polyglycerol backbone is not completely metabolized. Using the largest polyglycerol molecule allowed by FDA as the sole source of fat, decaplycerol was found in the urine of the test animals, yet we do not know whether this finding represents excesses or the non-metabolized portion. In any event, all products appeared to be non-toxic. The medical and pharmaceutical applications of the polyglycerols and the polyglycerol esters are an extension of the edible applications of these compounds, where the same multi-functional characteristics can be utilized in medical formulations. In addition to their uses as emulsifiers, solvents, and carriers for medications, the polyglycerol esters have demonstrated their unique solubility for carrying lipid in various metabolic applications*. In a conversation with W. C. Luscher, MD (April 1991) the polyglycerol esters have acted as substitutes or as having a sparing action for patients with pancreatic insufficiency and bile acid insufficiency.

The medical and pharmaceutical applications of the polyglycerols and

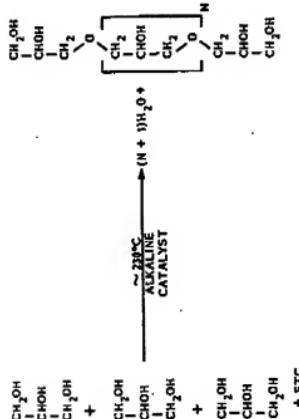


FIGURE 1. Preparation of polyglycerols.

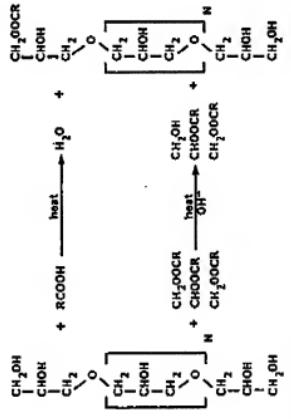


FIGURE 2. Preparation of polyglycerol esters.

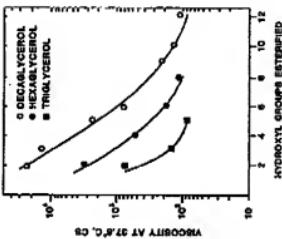


FIGURE 1. Effect of triglyceride ester on hydroxyl group estimation at 270°C.

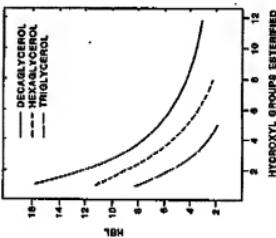


FIGURE 2. Effect of triglyceride ester on hydroxyl group estimation at 160°C.

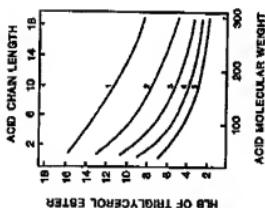


FIGURE 3. Effect of acid chain length and acid molecular weight on the HLB of triglyceride ester.

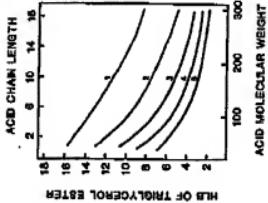


FIGURE 4. Effect of acid chain length and acid molecular weight on the HLB of triglyceride ester.

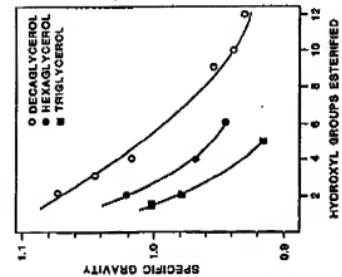
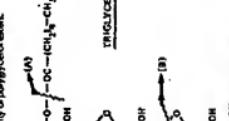


FIGURE 7. Specific gravity of polyglycerols.



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(B) : CLEAVAGE AT THE HYDROXYL GROUP IS POSSIBLY THE PREDOMINANT, UNUSUAL LABORATORY CONDITIONS AND IS STILL CONJECTURAL. UNUSUAL LABORATORY CONDITIONS EITHER LINKEAGE BECAUSE DRAMATIC SOLUBILITY WITH RESPECT TO EFFECT OF CLEAVAGE. INTRACELLULAR CLEAVAGE MAY PROBABLY NOT OCCUR SINCE CELLS REQUIRE ENERGY FOR METABOLISM OF POLYGLYCEROL. MOREOVER, IT IS EXCRETED DIRECTLY BEING METABOLIZED AS AN ENERGY SOURCE.

FIGURE 8. Possible modes of cleavage of polyglycerols and polyglycerol esters during metabolism. ■ Living system.

polyglycerol esters are practically in their infancy. What has been done thus far is merely the extension of the edible applications. The future will see the medical, pharmaceutical and health care field because of their versatility and unique physical and chemical characteristics, which can be programmed at will to give the specific functionality desired.

Polyglycerols and polyglycerol esters have made a marked penetration into the medical, pharmaceutical and health care field because of their versatility and unique physical and chemical characteristics, which can be programmed at will to give the specific functionality desired.

Grundy and Ahrens and others have used polyglycerol esters, notably the tri- and hexadecyl esters, as emulsifiers in special diets to solubilize and emulsify fat and cholesterol¹¹. Such emulsions have proven to be very satisfactory in carrying the fat and cholesterol in a uniform and stable state. These polyglycerol esters have been suggested to the pharmaceutical field as a unique class of emulsifiers, which are suitable for oral/enteral preparations where fat, cholesterol or other medication is to be solubilized and/or carried. The esters are liquid and the sterates are solid. Depending upon the type of product involved, one can select the specific polyglycerol ester best suited for the functionality. For example, the sterates are good solvents for cholesterol and other steroids and fat compounds. The sterates are good emulsifying agents and best suited for creams and ointments where aeration and volume is desired.

Kabara and co-workers in a series of publications have shown that the polyglycerol sterates have anti-microbial properties¹². Such anti-microbial properties are at an optimum with lauric acid and fall off on either side of the fatty acid chain length. The anti-microbial properties of the polyglycerol sterates progressively increase as the molecular weight of the polyglycerol increases. Thus, tri-, hexa and decadecyl laurates show progressive greater anti-microbial power. The number of free hydroxyls apparently enhances the anti-microbial ability of the laurate ester.

In this connection the recent data that is beginning to be reported in the literature appear to point to the excess of the production of bile acids and their conjugates with colon tissues over prolonged periods of time. This increased excretion appears to increase the incidence of colon cancer. Particularity in diets rich in fat, especially polyunsaturated fat, the incidences appear to be greater than that with diets having low fat content. If the polyglycerol esters can serve as a bile acid replacement and/or a sparing action, then they may be able to reduce the need for excessive bile acid production and the excessive concentrations appearing in the intestinal tract. Certainly the alternatives to the production and presence of high concentrations of bile acid in the colon should be in reducing the incidence of colon cancer. We shall wait to see whether polyglycerol esters can play a useful role in this area.

This good solvent characteristic of the polyglycerol esters for cholesterol has prompted some investigations to consider them not only as carriers and solvents for cholesterol, but also as possible agents for regression and solubilization of atherosms and plaque regression. W. G. Linchich, MD and others (April 1961) have found polyglycerol esters, notably and tridecyl monoglycero- and oleo-, to increase fat absorption through the intestinal wall markedly enhancing fat utilization in patients requiring fat or caloric sup-

plementation. Linuscheer also found that in patients deficient in or devoid of bile acids and pancreatic lipase, the polyglycerol esters were able to alleviate and/or show sparing action for these substances. The possibility that polyglycerol esters may possibly substitute bile acids and pancreatic lipases, suggests a number of areas of medical application, but much more clinical evidence is needed before we can arrive at a decision. The presence of polyglycerol esters in food products, however, may prove to be very helpful to patients having such deficiencies in bile acid and pancreatic lipase secretions.

In a conversation S.A. Hastings, J. Sale and others (December 1960) have noted the beneficial effect of polyglycerol esters, notably the triglycerid mono-caprylate and the di- α -glycerol mono-laurate in the absorption and transport mechanism in humans. In this way their work is collaborative to that carried out by Linuscheer and extends the area of availability of the polyglycerol esters. Hopefully other experimental data will become available to confirm other such unique uses of the polyglycerol esters.

The anti-microbial, emulsifying and solvent action of polyglycerol caprylates and laurates presents the possibility that such products can be considered as emulsifiers and protective agents for intravenous preparations, where sterility and protection against bacterial infection is always a desired state. Alone or with 85% propylene glycol, such polyglycerol laurates may well serve to improve present parenteral emulsions.

In the area of dietary formulations when caloric restriction is required,

the polyglycerol esters can serve as hybrid fats or as low calorie food product.

Kaunitz and Babayan demonstrated that polyglycerol esters are safe and non-toxic, even when used as the sole source of fat in a balanced diet. Babayan has postulated that such polyglycerol esters can play the role of a diabetic fat not only because the caloric value of the polyglycerol monostearates is in the range of 6-5.5 calories, but also because one can formulate products devoid of fat or very low level of fat, and yet give the impression that one is eating a rich, fatty food. The palatability and safety factor of such products is very acceptable.

Some questions have been raised by Michael and Coats whether the polyglycerol backbone is metabolized. Our data submitted to the FDA, for the clearance of such products in food use, showed that polyglycerols are completely metabolized. In the event, however, that the contention of Michael and Coats proves to be valid, such polyglycerol monostearates would have less than 2 calories/g instead of 6-5.5 calories/g. Thus, these low caloric emulsifiers would be even better suited for low caloric dietary products.

All in all, the polyglycerol esters for consideration as a medical and

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